

We claim:

1. A lipid-drug complex for subcutaneous administration comprising:
at least one lipid molecule; and
at least one drug molecule having low aqueous solubility within a neutral pH
5 range.
2. The lipid-drug complex of Claim 1, wherein the neutral pH range includes a
range near pH 5.0 to about pH 8.
- 10 3. The lipid-drug complex of Claim 1, wherein the lipid and drug molecules are
associated as a complex at a molar ratio of lipid-to-drug that is within a range of about 3:1 to
about 100:1.
4. The lipid-drug complex of Claim 1, wherein the drug substantially dissociates
15 from the lipid-drug complex within a pH range from about pH 5.0 to about pH 8.
5. The lipid-drug complex of Claim 1, wherein the lipid-drug complex is a
liposome.
- 20 6. The lipid-drug complex of Claim 1, wherein the liposome is a unilamellar
liposome.
7. The lipid-drug complex of Claim 1, wherein the drug is an anti-viral drug.
- 25 8. The lipid-drug complex of Claim 1, wherein the drug is an anti-HIV drug.
9. The lipid-drug complex of Claim 1, wherein the drug is indinavir, saquinavir,
nelfinavir, or tenofovir disoproxil fumarate.
- 30 10. The lipid-drug complex of Claim 1, wherein the drug is an anti-fungal drug.
11. The lipid-drug complex of Claim 1, wherein the drug is an anti-bacterial drug.

12. The lipid-drug complex of Claim 1, wherein the drug is an immunomodulatory drug.
13. The lipid-drug complex of Claim 1, wherein the drug is an anticancer drug.
- 5 14. The lipid-drug complex of Claim 1, wherein the drug inhibits the growth of breast cancer.
- 10 15. The lipid-drug complex of Claim 1, wherein the lipid includes one or more of phospholipids, sphingolipids, cardiolipins, spingomyelin, glycolipids, gangliosides, cerebroside, cholesterol, fatty acids, PEG derivatized lipids, monoglycerides, diglycerides, triglycerides.
- 15 16. The lipid-drug complex of Claim 1, wherein the lipid-drug complex is about 30 to about 150 nanometers in diameter.
17. The lipid-drug complex of Claim 1, wherein the lipid-drug complex is about 50 to about 80 nanometers in diameter.
- 20 18. A method for producing a lipid-drug complex comprising:
selecting one or more drugs for incorporation into lipid-drug complexes;
selecting one or more lipids or lipid-soluble compounds for forming lipid-drug complexes;
combining the one or more selected drugs and the one or more selected lipids
25 or lipid-soluble compounds in an environment conducive to formation of lipid-drug complexes.
- 30 19. The method of claim 18 wherein combining the one or more selected drugs and the one or more selected lipids or lipid-soluble compounds in an environment conducive to formation of lipid-drug complexes further includes:
adding the selected one or more drugs to a first solvent;
adding the selected one or more lipids or lipid-soluble compounds to a second solvent such that the one or more lipids or lipid-soluble compounds do not self-aggregate;

combining the first and second solvents containing the selected one or more drugs and the one or more lipids or lipid-soluble compounds;

removing the first and second solvents; and

resuspending the selected one or more drugs and the selected one or more
5 lipids or lipid-soluble compounds in aqueous, neutral pH solution.

20. The method of Claim 18 wherein combining the one or more selected drugs and the one or more selected lipids or lipid-soluble compounds in an environment conducive to formation of lipid-drug complexes further includes:

10 adding the selected one or more drugs to a first solvent;

adding the selected one or more lipids or lipid-soluble compounds to a second solvent such that the one or more lipids or lipid-soluble compounds do not self-aggregate;

combining the first and second solvents containing the selected one or more drugs and the one or more lipids or lipid-soluble compounds;

15 removing the first and second solvents; and

resuspending the selected one or more drugs and the one or more lipids or lipid-soluble compounds in aqueous, neutral pH solution.

21. The method of Claim 18 wherein combining the one or more selected drugs
20 and the one or more selected lipids or lipid-soluble compounds in an environment conducive to formation of lipid-drug complexes further includes:

adding the selected one or more drugs to a first solution at a pH lower than 6.0; and

adding the selected one or more lipids or lipid-soluble compounds in a
25 buffered, second solution to first solution.

22. The method of Claim 18 wherein combining the one or more selected drugs and the one or more selected lipids or lipid-soluble compounds in an environment conducive to formation of lipid-drug complexes further includes:

30 adding the selected one or more drugs to a first solution;

adding the selected one or more lipids or lipid-soluble compounds to a second solution at a temperature such that the one or more lipids or lipid-soluble compounds do not self-aggregate; and

combining the first and second solutions and lowering the temperature to a temperature at which the lipids self-aggregate.

23. The method of Claim 18 wherein combining the one or more selected drugs
5 and the one or more selected lipids or lipid-soluble compounds in an environment conducive to formation of lipid-drug complexes further includes:

adding the selected one or more lipids or lipid-soluble compounds to a solution in which the one or more lipids or lipid-soluble compounds self-aggregate; and

10 adding to the solution the selected one or more drugs to be taken up by the lipid aggregates to form lipid-drug complexes.

24. The method of Claim 18, wherein the lipid-drug complex is a liposome.

25. The method of Claim 18, wherein the liposome is an unilamellar liposome.
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26. The method of Claim 18, wherein the drug is an anti-viral drug.

27. The method of Claim 18, wherein the drug is an anti-HIV drug.

20 28. The method of Claim 18, wherein the drug is indinavir, saquinavir, nelfinavir, or tenofovir disoproxil fumarate.

29. The method of Claim 18, wherein the drug is an anti-fungal drug.

25 30. The method of Claim 18, wherein the drug is an anti-bacterial drug.

31. The method of Claim 18, wherein the drug is an anti-cancer drug.

32. The method of Claim 18, wherein the drug inhibits the growth of breast
30 cancer.

33. The method of Claim 18, wherein mixing the drug and lipids occurs within a range of lipid-to-drug molar ratio from about 3:1 to about 100:1.

34. The method of Claim 18, wherein the lipid includes one or more of phospholipids, sphingolipids, cardiolipins, spingomyelin, glycolipids, gangliosides, cerebroside, cholesterol, fatty acids, PEG derivatized lipids, monoglycerides, diglycerides, triglycerides.

35. The method of Claim 18, wherein the lipid-drug complex is about 30 to about 150 nanometers in diameter.

36. The method of Claim 18, wherein the lipid-drug complex is about 50 to about 80 nanometers in diameter.

37. The method of Claim 18, wherein the solvent is an aqueous solvent.

38. The method of Claim 18, wherein the organic solvent is selected from the group consisting of dimethyl sulfoxide, methanol, ethanol, propanol, propane glycol, butanol, isopropanol, pentanol, pentane, a fluorocarbon, and an ether.

39. A method for preferentially delivering an anti-HIV drug having low aqueous solubility within a neutral pH range to lymphoid cells in a lymphoid tissue of a mammalian subject infected with HIV, comprising:

injecting into the mammalian subject infected with HIV, a lipid-drug complex comprising a lipid bilayer that comprises the anti-HIV drug that has low aqueous solubility at about neutral pH, such that the lipid-drug complex arrives at the lymphoid tissue via lymphatic vessels, and the anti-HIV drug is thereby preferentially delivered to the lymphoid tissue.

40. The method of Claim 39, wherein the lymphoid tissue is a lymph node.

41. The method of Claim 39, wherein the lymphoid tissue is spleen, thymus, or mucosal-associated lymphoid tissue.

42. The method of Claim 39, wherein the lipid-drug complex is a liposome about

30 to about 150 nanometers in diameter.

43. The method of Claim 39, wherein the anti-HIV drug is indinavir, saquinavir, nelfinavir, or tenofovir disoproxil fumarate.

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44. The lipid-drug complex of Claim 39, wherein the molar ratio of lipid-to-drug in the lipid-drug complex, within a neutral pH, is about 3:1 to about 10:1.

45. The lipid-drug complex of Claim 39, wherein the molar ratio of lipid-to-drug
10 in the lipid-drug complex, within a neutral pH range, is about 5:1 to about 7:1.